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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/901,484	07/09/2001	Daniel Cohen	GEN-T111XC3D2	6608

23557 7590 06/23/2004

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 06/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/901,484	COHEN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. The current application claims priority to a series of cases dating back to 1997. However, the claims are not given priority to applications 08/996,306 and 60/099,658 because in the current application SEQ ID NO: 179 is 56,520 nucleotides while in those parent applications, the largest sequences were 56,516 nucleotides. Consequently, there is no possibility that these applications provide full descriptive support for SEQ ID NO: 179, and priority to these applications is denied. Therefore, for purposes of prior art, the priority date of this application is limited to 09/218,207, filed December 22,1998, which provides the full 56,520 nucleotides of SEQ ID NO: 179.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 54 and 55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in

possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

Claims 54 and 55 are drawn to knockouts of the PGC-1 gene. So the genus includes cells in which the PGC-1 gene is entirely absent. This large genus therefore includes variants for which no written description is provided in the specification in a genus which comprises hundreds of millions of different possibilities, due to the knockout language. Here, no common element or attributes of the sequences remaining after knockout are disclosed. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally

> known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of mammals comprising knockouts of the PGC-1 gene lacks any specific structure. This definition is precisely the situation of naming a type of material which is generally known to likely exist, but is in the absence of knowledge of the material composition and fails to provide descriptive support for the generic claim.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely by its name as a knockout, without any definition of the particular knockouts claimed.

In the instant application, SEQ ID NO: 179 is described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nonhuman mammals with knockouts in the PGC-

1 gene. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 50-52, 56-58 and 61-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Gu et al (Proc. Natl. Acad. Sci. (1991) 88:5867-5871) (as shown in Genbank Accession No. M68941 (April 27, 1993)).

Gu et al teaches an isolated polynucleotide sequence which has a contiguous region with a 100% match with 38 contiguous nucleotides of SEQ ID NO: 179 in the region from nucleotides 13206-14150 of SEQ ID NO: 179.

```
Query: 13772  acagatttttggcagatgacttgggaacaaggctcctc 13809
              ||||||||||||||||||||||||||||||||||||
Sbjct: 2974   acagatttttggcagatgacttgggaacaaggctcctc  3011
```

With regard to claim 51, Gu teaches the sequence was placed in the pTrp vector (see page 5870, column 1).

With regard to claim 52, Gu teaches an E. coli host cell comprising the vector (see page 5870, column 1)).

With regard to claim 56, Gu teaches radiolabeling of the target nucleic acid sequences (see page 5868, column 1).

With regard to claims 57 and 58, Gu teaches screening of a cDNA library, where the cDNAs were attached to a solid support in a random array (see page 5868, column 1).

With regard to claims 61-63, Gu teaches the sequence as disclosed above.

5. Claims 50 and 59--66 are rejected under 35 U.S.C. 102(b) as being anticipated by Weier et al (Hum. Genet. (1991) 87:489-494).

Weier et al teaches an isolated human chromosome 8, which was flow sorted to purify the sequence (see abstract and page 490, column 2). The current PG-1 sequences are all derived from chromosome 8 as admitted by the specification at page 28. So chromosome 8 is a sequence of more than 500 nucleotides which comprises SEQ ID NO: 179. The chromosome comprises the complement inherently.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gu et al (Proc. Natl. Acad. Sci. (1991) 88:5867-5871) in view of Capecchi et al (Science (1989) 244:1288-1292).

Gu et al teaches an isolated polynucleotide sequence which has a contiguous region with a 100% match with 38 contiguous nucleotides of SEQ ID NO: 179 in the region from nucleotides 13206-14150 of SEQ ID NO: 179.

```
Query: 13772  acagatttttggcagatgacttgggaacaaggctcctc 13809
               |||||||||||||||||||||||||||||||||||||
Sbjct: 2974   acagatttttggcagatgacttgggaacaaggctcctc  3011
```

With regard to claim 51, Gu teaches the sequence was placed in the pTrp vector (see page 5870, column 1).

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With regard to claim 56, Gu teaches radiolabeling of the target nucleic acid sequences (see page 5868, column 1).

With regard to claims 57 and 58, Gu teaches screening of a cDNA library, where the cDNAs were attached to a solid support in a random array (see page 5868, column 1).

With regard to claims 61-63, Gu teaches the sequence as disclosed above.Genbank Accession No. N39909 does not teach formation of a disrupted host mammalian cell.

Capecchi teaches the use of homologous recombination to form host cells and mammals (see page 1280, figure 1, for example).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to screen the sequence of Gu for its functional activity using the homologous recombination method of Capecchi since Capecchi states "Targeted disruption of these genes may not only reveal the phenotypes associated with inactivation of the individual genes, but through epistasis and molecular analyses, may also help define the developmental network controlling early mouse morphogenesis (see page 1292, column 1)." Thus, an ordinary practitioner, interested in identifying what phenotype is associated with the sequence of the sequence of Gu would have been motivated by Capecchi to use targeted disruption in order to define the phenotype of the gene with which the sequence of Gu is associated.

Response to Arguments

9. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637